DFW AF/3743/#

TRANSMITTAL OF APPEAL BRIEF (Large Entity)	Docket No. 2035.706

In Re Application Of: **Wisniewski et al.**

Serial No.	Filing Date	Examiner	Group Art Unit
08/895,936	July 17, 1997	John K. Ford	3743

Invention: **FREEZING AND THAWING VESSEL WITH THERMAL BRIDGE FORMED BETWEEN HEAT EXCHANGE MEMBERS**

TO THE COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on

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Signature

Dated: June 10, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Wisniewski et al.	**Group Art Unit:**	3743
Serial No.:	08/895,936	**Examiner:**	John K. Ford
Filed:	July 17, 1997	**Appeal No.:**	

Title: FREEZING AND THAWING VESSEL WITH THERMAL BRIDGE FORMED BETWEEN HEAT EXCHANGE MEMBERS

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on June 10, 2004.

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Date of Signature: June 10, 2004

To: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
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Brief of Appellant

Dear Sir:

This is an appeal from a final rejection, dated February 24, 2004, rejecting claims 69-116 and 118-123, a portion of the claims pending in the above-identified application.

Real Party In Interest

This application is assigned to **Integrated Biosystems, Inc.** by virtue of an assignment executed on October 1, 1997 by the co-inventors and recorded with the United States Patent and Trademark Office on reel 9068 and frame 0033. Therefore, the real party in interest is **Integrated Biosystems, Inc.**

Related Appeals and Interferences

To the knowledge of the Appellant, Appellant's undersigned legal representative, and the applicants, there are no interferences which will directly affect or be directly affected by or having a bearing on the Board's decision in the instant appeal. There are, however, two other appeals that may be directly affected by or have a bearing on the Board's decision in the instant appeal. All of these appeals involve the same Examiner. These appeals involve the following applications:

Serial Number No. 10/057,610, notice of appeal filed April 19, 2004.
Serial Number No. 09/881,909, notice of appeal filed April 19, 2004.

Status of Claims

This patent application was filed on July 17, 1997. As filed, the application included thirty-five (35) claims, of which one (1) was an independent claim (i.e. claim 1).

In an initial Office Action dated November 20, 1998[1], claims 1-5, 9, 10, 14-20, 22-30 and 33 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 4,793,151 to Masel ("Masel") in view of U.S. Patent No. 2,610,034 to Lundvall ("Lundvall"); claims6- 8 were rejected under 35 U.S.C. §103(a) as being unpatentable over Masel in view of Lundvall as applied to claim 1 and further in view of U.S. Patent No. 4,296,612 to Allo ("Allo"); claims 11 and 31 were rejected under 35

[1] An Office Action dated October 29, 1998 initially issued but was supplemented by the Examiner with the Office Action dated November 20, 1998.

U.S.C. §103(a) as being unpatentable over Masel in view of U.S. Patent No. 3,453,416 to Mekjean ("Mekjean"); and claim 21 and 35 were rejected under 35 U.S.C. §103(a) as being unpatentable over Masel in view of U.S. Patent No. 4,712,607 to Lindemans ("Lindemans"); claims 12, 32 and 34 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 4,893,670 to Joshi in view of U.S. Patent No. 3,934,618 to Henderson. In this Office Action, claim 13 was objected to as being dependent upon a rejected base claim, but the Office indicated that it would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In Appellant's response dated March 19, 1999, claim 21 was cancelled and claim 1 was amended.

In a second Office Action dated June 21, 1999, the Office subjected the application to an election requirement under 35 U.S.C. §121. In Appellant's response dated July 21, 1999, Appellant elected the species shown in Figure 5 and identified claims 1-20 and 22-35 to read on this species.

In a third Office Action dated October 15, 1999, claims 1-20 and 22-35 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (e.g. the Office pointed to the words "heat exchange member" and "biopharmaceutical product"); claims 1-20 and 22-35 were rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over the Wisniewski and Wu article entitled "Large-scale freezing and thawing of Biopharmaceutical Products and the underlying use known to other of the experimental pilot-scale equipment"; claims 1-20 and 22-35 were rejected under 35 U.S.C. § 103(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,220,954 to Longardner et a ("Longardner"); and claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over Longardner as applied to claim 1 above, and further in view of U.S. Patent No. 2,391,876 to Brown. In Appellant's response dated April 13, 2000, claims 1-20 and 22-35 were cancelled and claims 36-68 were added.

Appellant also submitted the Declarations of Chris J. Burman, V. Bryan Lawlis, Jr., and David A. Vetterlein, each of whom has at least around two decades of experience in the industry, to unanimously support the definition of "biopharmaceutical products" as it is understood in the art.

In a fourth Office Action dated July 5, 2000, the Office refused newly submitted claims 36-68 and considered the amendment filed April 18, 2000 as non-responsive because the claims were not readable on the elected invention. In Appellant's response dated August 30, 2000, which arose out of an in-person interview with the Examiner on August 1, 2000, claims 41-43, 63 and 67 were canceled and claim 36 was amended. Appellant submitted a second response dated December 7, 2000 in which they canceled claims 53, 54, and 56 and amended claim 47.

In a fifth Office Action dated December 19, 2000, the Office requested a listing of claims readable on the elected species pertaining to newly presented claims 36-68. In Appellant's response dated April 18, 2001, claims 36-40, 44-52, 55-62, 64, 65 and 68 were elected.

In a sixth Office Action dated September 6, 2001, which the Examiner designated as final, claims 36-40, 44-62, 64-66 and 68 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point our and distinctly claim the subject matter which applicant regards as the invention because of the vague terms "thermal bridge" and "biopharmaceutical product" and claims 49-54, 59-62 and 64-66 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite because the Office considered these claims to contain feature not found in the elected species of Figure 5. With respect to the prior art rejections in this Office Action, claims 36-40, 44-62, 64-66 and 68 were rejected under 35 U.S.C. §103(a) as obvious over the 1992 Wisniewski and Wu article in view of U.S. Patent No. 3,308,552 to Kaufman et al ("Kaufman"), Longardner, and Great Britain Patent No. 845,576 to Richelli ("Richelli"); claim 47 was rejected under 35 U.S.C. §103(a0 as being unpatentable over the prior art as

applied to claim 36 and further in view of Brown or U.S. Patent No. 2,915,292 to Gross ("Gross"); and claims 49-54 were rejected under 35 U.S.C. §103(a) as being unpatentable over any of the prior art as applied to claim 36, and further in view of U.S. Patent No. 5,535,598 to Cothern ("Cothern"). In Appellant's response dated January 7, 2002, claims 36-40, 44-62, 64-66 and 68 were canceled and claims 69-89 were added. Appellant filed a supplemental response dated January 24, 2002 in response to a telephonic interview with the Examiner on January 4, 2002. In this supplemental response, appellant submitted a Declaration of Richard Wisniewski dated January 23, 2002 ("First Declaration of Richard Wisniewski") to assist the Examiner in his understanding of the differences between the present invention and the cited prior art, especially the device ("the Genentech device") disclosed in the 1992 Wisniewski and Wu article.

In a seventh Office Action dated July 12, 2002, claims 69-87, which were directed to apparatus claims, were withdrawn from consideration by the Examiner and claims 88 and 89 were examined. In this Office Action, claims 88 and 89 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite again because of the terms "thermal bridge" and "biopharmaceutical product." Claims 88 and 89 were also rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over the 1992 Wisniewski and Wu article, alone, or further in view of U.S. Patent No. 3,550,393 to Euwema ("Euwema"), Cothern, the 1986 Kalhori and Ramadhyani article[2], U.S. Patent No. 1,874,578 to Morrison ("Morrison"), and Japanese Patent No. JP 57-58087 to Nakao ("Nakao"), or any of the prior art as applied to claim 88 and 89 and further in view of Cothern. In Appellant's response dated October 7, 2002, claims 90-123 were added.

In an eighth Office Action dated January 29, 2003, the Office issued an election requirement under 35 U.S.C. §121. In Appellant's response dated February 28, 2003,

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[2] Entitled: "Studies on heat transfer from a vertical cylinder, with or without fins, embedded in a solid phase change medium."

claim 117 was canceled, claims 101 and 104 were amended and Appellant elected to pursue claims 88-89, 969, 101, 105-116 and 118-119.

In a ninth Office Action dated June 16, 2003, the Office did not reject any of the claims, but instead questioned the adequacy of Appellant's disclosures to the Patent Office. Appellant responded to these bald accusations on July 10, 2003.

More than seven and a half months after the ninth Office Action[3], the Office issued a tenth and final Office Action dated February 24, 2004, in which the Examiner maintained his rejections under 35 U.S.C. §112, second paragraph. In this final Office Action, claims 88, 89, 96, 105, 108-110, 112-115, 118 and 119 were rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over the 1992 Wisniewski and Wu article, turning also to U.S. Patent No. 984,052 to Voorhees ("Voorhees") and U.S. Patent No. 2,129,572 to Finnegan ("Finnegan") for additional support. These claims were also rejected under 35 U.S.C. §103(a) as obvious over the 1992 Wisniewski and Wu article in view of Euwema, Cothern, the 1986 Kalhori and Ramadhyani article, Morrison and Nakao. Claims 96, 105-110, 112-115, 118 and 119 were also rejected under 35 U.S.C. §103(a) as being unpatentable over (1) the combined teachings of the 1992 Wisniewski and Wu article and the 1986 Kalhori and Ramadhyani article, turning again to Voorhees and Finnegan for assistance; (2) the combined teachings of the 1992 Wisniewski and Wu article, the 1986 Kalhori and Ramadhyani article, Euwema, Cothern, U.S. Patent No. 2,114,642 to West, Morrison and Nakao; and (3) any of the prior art as applied above for these claims in view of the conceded prior art discussed on pages 1, line 22 to page 2, line 17 of the specification. Finally, claims 101, 111 and 116 were rejected under 35 U.S.C. §103(a) as being unpatentable over any of the prior art applied to claims 88, 110 and 115 above, and further in view of Gross or Brown.

[3] The Examiner's indication that any delay in pursuing an appeal is entirely applicants' responsibility not the Examiner's is simply not true.

A Notice of Appeal to the Board of Patent Appeals and Interferences was filed on April 19, 2004. The statue of the claims is therefore as follows:

Claims allowed:	None
Claims objected to:	None
Claims rejected:	88, 89, 96, 101, 105-116, 118 and 119
Claims canceled:	1-68, 117
Claims withdrawn:	69-87, 90-95, 97-100, 102-104, 120-123

Appellant is appealing the rejection of claims 88, 89, 96, 101, 105-116, 118 and 119.

Status of Amendments

Appellant proffered no response to the final Office Action dated February 24, 2004. The claims as set out in the Appendix include all prior entered amendments.

Summary of the Invention

Appellant's invention is directed to a method of processing a biopharmaceutical product. The method includes providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, the vessel having an interior cavity defined by an interior wall of the vessel and a heat exchange structure within the cavity, the heat exchange structure having one or more heat transfer members. The method also includes placing a medium comprising a biopharmaceutical product within the vessel; actively cooling the interior wall using a cooling fluid; and forming a thermal bridge within a gap between the heat transfer member and the interior wall by the medium wherein heat is transferred from the heat transfer member through the thermal bridge to the interior wall.

Issues

1. Whether the term "biopharmaceutical product" is ambiguous under 35 U.S.C. §112, second paragraph.

2. Whether the term "thermal bridge" is vague under 35 U.S.C. §112, second paragraph.

3. Whether any of the cited prior art, either alone or in combination, renders claims 88, 89, 96, 101, 105-116, 118 and 119 are patentable.

4. Whether Appellant satisfied its duty under Rule 56.

Grouping of Claims

Appellant respectfully submits that the claims do not stand or fall together. For example, claims 90 and 121 are grouped together as a separate group, claim 91 is a separate group, claim 99 is a separate group, and claim 95 is a separate group. Claims 101 and 111 are also a separate group. Each separate group includes additional features that provide a separate basis of patentability from independent claims 88 and 108 from which they depend.

Argument

A. The Terms "Biopharmaceutical Product" and "Thermal Bridge" Are Not Ambiguous Or Vague

1. The Term "Biopharmaceutical Product" Is Not Ambiguous

As noted, claims 88, 89, 96, 101, 105-116, 118 and 119 stand rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "biopharmaceutical product" ambiguous. Reversal of this rejection is respectfully requested.

Appellant did not provide a definition in the specification for the term "biopharmaceutical product." This term has a recognized meaning to those of ordinary

skill in the art. The specification provided a number of examples of the type of biopharmaceutical products that may be processed by the present invention. The term "biopharmaceutical product" as set forth in the Specification on page 20 includes, but is not limited to, proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product.

Appellant provided a definition of a "biopharmaceutical product" in an Amendment dated April 13, 2000 (in response to the third Office Action dated October 15, 1999, which was the first time the Examiner objection to the term "biopharmaceutical product") as "a product derived from biological sources that has an intended therapeutic application and whose manufacturing is or will be regulated by pharmaceutical or veterinary regulatory agencies." This definition is supported by the Declarations of Chris J. Burman, V. Bryan Lawlis, Jr., and David A. Vetterlein ("the Declarants"), who are persons of ordinary skill in the art.

Despite support of the aforementioned understanding of the term of "biopharmaceutical products" from three persons of ordinary skill in the art having over 72 years of experience in the biotechnology and biopharmaceutical industry, the Office erroneously complicated the well-recognized understanding of this term. For example, the Office sets forth an opinion in concluding that orange juice and milk are biopharmaceutical products. In particular, the Examiner makes an unsupported statement in the final Office Action on page 14 that "[b]lood *would probably* freeze more in the manner of orange juice or milk given its nearly macroscopic cellular nature whereas virus in a suitable buffer solution or water would freeze in the manner of pure or salty water." (emphasis added). Based on such reasoning and unsupported statements, the Office indicates that the definition offered by the Declarants "appears" to be unworkable. (See page 14 of the final Office Action). However, when not defined by an applicant in the specification, the words of a claim must be read, as they would be interpreted by those of

ordinary skill in the art, MPEP 2111.01, not by the Examiner himself or a hypothetical infringer, which is addressed in more detail below.

In the final Office action, the Examiner also suggests that nothing in the declarations address why one designing freezing equipment for biopharmaceutical products disclosed in the specification would not look to the art of freezing water, orange juice or solids suspended in liquids. To the contrary, this issue has been addressed numerous times in previous responses and in the specification. As provided in the specification, Appellant recognized, among other things, that the apparatus and method according to the aspects of the present invention are suited for use in processing biopharmaceutical products, as that term is understood by those of ordinary skill in the art. For example, the recited apparatus and method promotes uniform freezing at a rapid pace, which allows the biopharmaceutical product in the container to be frozen in as close to its native state as possible. (Specification, page 7, lines 17-19). Additionally, the present invention allows the freezing process to be done in a repeatable fashion so that a user can be assured that the freezing process is not causing batch-to-batch variations in the product. (Specification, page 7, lines 19-21).

Appellant respectfully submits that improper processing of biopharmaceutical product by, such as, for example, freezing and thawing, destroys biopharmaceutical products. In contrast, other products, such as, for example, orange juice, milk, water, particulate materials, and comestibles do not have the same processing concerns as biopharmaceutical products. Therefore, such products as orange juice, milk, water, particulate materials and comestibles, which do not require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage, are not included in the definition of biopharmaceutical products. In particular, the method or apparatus used to process (e.g. freeze or thaw) these other products is not critical and will not destroy these other products. (See Amendment and Response dated January 7, 2002).

Appellant, however, recognizes that, for example, a "buffer solution" can indeed be a biopharmaceutical product depending upon the contents of such a solution. In lab chemistry, buffers are associated with the maintaining of certain pH levels, while biopharma vocabulary (which is relevant to this application) uses the term buffers very broadly, including buffers with proteins (like Human Serum Albumin) or amino acids (multiple amino acids are used, for example, lysine or arginine) clearly having biomolecules which can be damaged by improper freezing. It is readily apparent that buffer solutions, which are biologically based, may indeed be regulated and be a biopharmaceutical product. Appellant respectfully submits that if, for example, a particular buffer solution is not derived from biological sources nor regulated by FDA, then it would not be considered a biopharmaceutical product under the aforementioned understanding of the term. The list of potential biopharmaceutical products provided in the specification sets forth examples of products, which may be biopharmaceuticals. Because the term has a recognized meaning within the art, it is readily apparent to one of ordinary skill in the art what the term "biopharmaceutical product" means.

Therefore, Appellant respectfully traversed the opinions set forth by the Office in the Office Actions that orange juice, milk, water, comestibles, particulate materials and any other non-biopharmaceutical products relied upon by the Office Action are considered a biopharmaceutical product and that vessels that freeze such materials are relevant to the delicate preservation of biopharmaceutical products. Appellant also requested the Office to support, by a reference or affidavit pursuant to M.P.E.P. § 2144.04, its position and opinion or in contradiction to the above definition in the Declarations by three persons of ordinary skill in the art. (See Amendment and Response dated January 7, 2002). Specifically, Appellant requested that the Office show that products such as orange juice, milk and comestibles require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage. The Office ignored this request. Instead, the Examiner maintains his rejection and continues to rely on his own personal opinion and knowledge, without providing any additional support. (See pages 11-13 of the final Office Action).

Appellant respectfully submits that one of ordinary skill in the art is capable of distinguishing and classifying which products are and are not biopharmaceutical products based on the above definition, as evidenced by, for example, the Declarants classification of milk and orange juice as not being pharmaceutical products in their Declarations. For example, one of ordinary skill in the art is capable of determining which proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product are considered a biopharmaceutical product under the above definition.

Finally, the reliance by the Office in the final Office Action (page 13) on an interpretation of a "would-be infringer" in rejecting the term "biopharmaceutical products" is improper. Under M.P.E.P. § 2173.02, definiteness of claim language must be analyzed in light of the content of the particular application disclosure, the teachings of the prior art and the claim interpretation that would be given *by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.* Appellant respectfully submits that the proper inquire is how "biopharmaceutical product" will be interpreted by a person of ordinary skill in the art, not by a "would be" infringer. Therefore, the Office, in maintaining the rejection of the term "biopharmaceutical products" on this basis, failed to follow this approach and, thus, the rejection is improper.

Accordingly, Appellant respectfully submits that the term "biopharmaceutical product" is not ambiguous and request withdrawal of this rejection.

2. The Term "Thermal Bridge" Is Not Vague

As noted, claims 88, 89, 96, 101, 105-116, 118 and 119 stand rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "thermal bridge" vague. Reversal of this rejection is respectfully requested.

The claims in the present invention specifically and clearly recite that a "thermal bridge" is formed "in a gap between said heat transfer member and said interior wall by said medium wherein heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to the interior wall being "actively cooled." Thus, a "thermal bridge" is not merely "any area where a thermally conditioned surface is in greater proximity to another surface", as suggested by the Examiner. Rather, a "thermal bridge", as claimed, requires heat to be transferred therethrough in a particular way, i.e. from the heat transfer member to the interior wall. This heat transfer results in a downward temperature gradient from the heat transfer member to the interior wall of the vessel, when the interior wall is actively cooled.

This definition is further reinforced by, and consistent with, the disclosure in the drawings and Specification. For example, the temperature profile in Figure 3(b), which is reproduced below, shows a downward temperature gradient from the heat transfer member to the interior wall of the vessel.

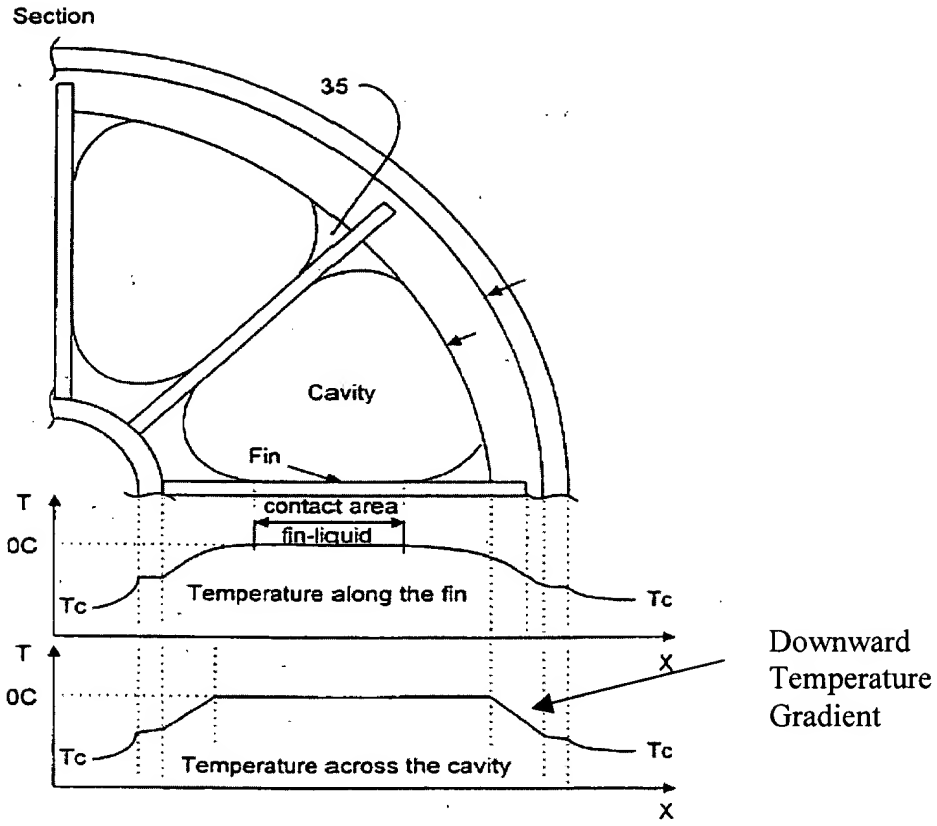

FIG. 3b

The Specification at pages 12 and 13 confirms that Fig. 3b occurs shortly after thermal bridges have begun to form while the interior wall is being "actively cooled". The Specification also enables persons of ordinary skill in the art to determine how the heat exchange structure must be positioned within the interior cavity in order to form a thermal bridge by the medium between one or more of the heat transfer members and the interior wall. Specifically, the Specification provides at page 6, lines 8-14 the following:

> In general, the system should be constructed such that the distance to be bridged by the thermal transport bridge will be a function of the thermal properties of the medium and the system, manufacturing requirements and construction processes used to build the system, and other relevant parameters of the system and components used. The size of the gap to be filled by the bridge can be determined through simple trial and error.

The Specification further provides, on page 6, lines 23-27, clear examples of the size of the gap. Specifically, the Specification states that in one aspect of the present invention, the optimum gap is less than 2 inches, preferably less than 1 inch, even more preferably less than ¼ inch, and most preferably less than 1/8 inch.

In further support of the invention as claimed and to assist the Examiner in his understanding of the invention, Appellant submitted two declarations by Richard Wisniewski: (1) Declaration of Richard Wisniewski, dated January 23, 2002 ("First Wisniewski Declaration") and (2) Second Declaration of Richard Wisniewski, dated February 26, 2003 ("Second Wisniewski Declaration").

As supported by these declarations, Appellant respectfully submits that if, however, the gap between the heat transfer member and the interior wall is too large, a thermal transfer bridge will never form, even if the entire medium in the gap is frozen. (First Wisniewski Declaration, ¶6). If the gap is too large, then a location between the heat transfer member and the interior wall will have a higher temperature than the heat transfer member and the interior wall, even if the medium in the gap is frozen, and not a downward temperature gradient from the heat transfer member to the interior wall as as claimed and depicted in Fig. 3(b) of the present application. (First Wisniewski Declaration, ¶8). Thus, if the gap is too large, heat is not transferred from the heat transfer member through the medium in the gap to the interior wall. Rather, heat is transferred from the medium at a location in the gap to the interior wall and to the heat transfer member.

In other words, if the gap is too large, heat is being extracted from a location in the gap between the heat exchange member and the interior wall, not from the heat transfer member to the interior wall as required when a thermal bridge is formed. (First Wisniewski Declaration, ¶7). Thus, as compared to, for example, the downward temperature gradient from the heat transfer member to the interior wall shown in the temperature profile in Fig. 3(b), a temperature profile of a device, such as, for example,

the device disclosed in the 1992 Wisniewski and Wu article, would show the temperature gradually increasing after the fin to a location in the gap between the fin and the interior wall and then gradually decreasing towards the interior wall. (First Wisniewski Declaration, ¶7, Ex. B). In fact, even after the medium in the gap is frozen, the temperature at a location between the fin and the interior wall is still higher and heat is transferred from this location in the gap to both the fin and interior wall. (First Wisniewski Declaration, ¶¶8-9, Exs. C-D). Therefore, no thermal bridge wherein heat is transferred from said heat transfer member through said heat thermal bridge to said interior wall is formed by the device disclosed in the 1992 Wisniewski and Wu article.

The Examiner fails to recognize the heat transfer characteristics of a "thermal bridge" as claimed and as described in the Specification, shown in the drawings and supported by the declarations submitted during prosecution. The Examiner provided no proof, other than his own personal knowledge, opinion and his interpretation of "self-evident principles of heat transfer", to support his conclusion that a thermal bridge does not exist in the present invention or that the cited prior art inherently forms a thermal bridge, which is clearly contradictory to the Appellant's disclosure. However, "[i]t is never appropriate to rely solely on 'common knowledge' in the art without evidentiary support in the record, as the principal evidence which the rejection is based." MPEP 2144.03. In the instant case, the Examiner's assessment of alleged basic knowledge and common sense is not based on any evidence in the record and is simply not enough to support the rejection of the claims.

The Examiner has improperly referred to the term "thermal bridge" as an "ice bridge" since the beginning of prosecution. Specifically, the Examiner suggests that a "thermal bridge of ice will inherently form [in the device disclosed in the 1992 Wisniewski and Wu article] between the tip of the heat transfer fins and the interior of the container because they are the closest points to one another and both are actively cooled by circulating cooled silicon oil." (See final Office Action, page 27). In support of this statement, the Examiner points to the Voorhees patent, U.S. Patent No. 3,318,105 to

Burroughs et al ("Burroughs"), U.S. Patent No. 2,129,572 to Finnegan ("Finnegan"), and his own rendition of the device disclosed in the 1992 Wisniewski and Wu article on page 30 of the final Office Action. However, in each of these instances, the Examiner equates an ice bridge with ice that surrounds or builds up on, for example, the interior wall and heat transfer member and eventually joins in the gap between the two. The Voorhees patent states:

> In the first instance of course, ice forms separately about each freezing element, but if these elements be close together the ice surrounding these elements will soon coalesce into a single cake; and after this has occurred freezing will go on from the surface of the combination cake so formed. (Voorhees, col. 2, line 97 to col. 1, line 5).

The Burroughs patent shows ice build up in an ice tray, having no interior structure, in a refrigerator and the Finnegan patent shows frozen build up on the interior wall and the interior structure and meeting in the middle of the space between these two structures. Moreover, Voorhees, Burroughs and Finnegan patents are not directed to processing biopharmaceutical products (but rather water and comestibles) and do not recognize the problems of processing such products.[4]

The Examiner's own rendition of the device disclosed in the 1992 Wisniewski and Wu article on page 30 of the final Office Action also shows build up on both the fins and the interior wall of the container that meet in the middle. However, ice build up on two surfaces that meet in the middle of the gap is not a "thermal bridge" as defined by the present invention and does not create a downward temperature gradient from the heat transfer member to the interior wall, as required by the claims. (See First Wisniewski Declaration, ¶7-9, Exs. B-D). In fact, such an ice formation from both surfaces towards

[4] Therefore, the Examiner's application of the "science" in Voorhees, Burroughs and Finnegan on page 29 of the Office Action to the device disclosed in the 1992 Wisniewski and Wu article is improperly because there is no motivation or suggestion to look at references that freeze water and comestibles to solve any problems relating to the critical method of processing biopharmaceutical products.

the middle requires a higher temperature in the middle and, thus, does not meet the terms of the claims.

Finally, the Examiner stated, numerous times throughout prosecution, his disbelief that a thermal bridge actually forms and requested experimentation, in the form of computer generated results" by the Applicants of the present invention and the device disclosed in the 1992 Wisniewski and Wu article. With respect to the Examiner's request that Appellant conduct experiments and provide "computer generated results" on its own device, Appellant respectfully submits that the Specification describes a simulation for the system disclosed and provides the parameters of the simulation, including the temperatures of the fins, the coolant and the wall. Fig. 3b is represented in the Specification as the result of this simulation.

> Figure 3b illustrates a simulation for the system shortly after thermal bridges 35 have begun to form. In this simulation, the material properties of 315 stainless steel were used for the container and the fins, and the coolant temperature was –45 °C. The temperature of the liquid was –0.2°C, the temperature of the fin in contact with the liquid was close to –0.2°C, and the temperature of the portion of the fin in contact with the frozen product was declining toward the temperature of the wall. The temperature of the wall was within 2-5°C of the temperature of the coolant. Specification, page 12.

Therefore, the Examiner's request is unnecessary and cumulative to what was already provided and supported by the Specification. For some unknown reason, the Examiner has ignored the same.

With respect to the Examiner's request that Appellant test the device disclosed in the 1992 Wisniewski and Wu article, Appellant has repeatedly informed the Examiner that this device is owned by Genentech, a customer in certain respects and a competitor in other respects. Although one of the inventors worked on this device back in the early 1990s as an employee of Genentech, he has provided as much information as he remembers about the device in the form of declarations. Despite the fact that this

inventor worked on this device over a decade ago, the Examiner continues to assert that he is not being forthcoming.

There is absolutely no requirement for an applicant or their assignee to submit information that is unknown and/or not readily available. Accordingly, Appellant's previous response that this information and experimentation of a device they have no control over is unknown and not readily available should be considered and accepted as a complete reply to the Examiner's request. 37 C.F.R. §1.105(a)(3). Moreover, a demand or request for experimentation of an invention or a prior art device is not the type of information, listed in 37 C.F.R. §1.105(a), that an Examiner may require or request from an application or assignee. A further discussion of the Examiner's requests during the course of this prosecution will be discussed in more detail below.

Accordingly, Appellant respectfully submits that the term "thermal bridge" is not vague and request withdrawal of this rejection.

B. The Claims Are Patentable Over The Cited Prior Art

Claims 88, 89, 96, 101, 105-116, 118 and 119 stand rejected over various combinations of at least eleven (11) different prior art references. However, as noted below, none of these references disclose or suggest the formation of a thermal bridge such that "heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to "actively cooling" the interior wall, as required by all of the claims. Further, all but one of the references relied upon by the Examiner disclose the processing of products unrelated to biopharmaceutical product and, thus, do not recognize the processing concerns of biopharmaceutical products. Further all of the references describe completely different methods of processing products using completely different principles. Therefore, there is simply no motivation or suggestion to support a combination of any of these references.

In fact, the Examiner, in the final Office Action supports this conclusion that there is no motivation or suggestion to combine any of the cited references by admitting the following, which occurs throughout the final action:

> The Examiner . . . does not believe that there is anyone who can model or calculate these temperature profiles without the aid of sophisticated computers and/or experimental work. . . .The processes of modeling natural convection and moving-front phase change occurring together with sub-cooling is, to the Examiner's knowledge, is state of the art or beyond the state of the art in numerical solutions on computers. See Final Office Action, page 8.
>
> It is respectfully submitted that these freezing phenomena are so complex that no human being including one with nearly 30 years of experience can accurately predict such results. Purporting to have such ability only diminishes ones credibility. See Final Office Action, page 10.
>
> Thus, researchers, other than Mr. Wisniewski, state that accurate modeling of phase change heat transfer in tanks with finned element such as shown in Figure 3 of the K&R article can only be done by computers or by direct empirical measurement. See Final Office Action, page 11.
>
> [T]he temperature distribution must either be measured or generated by very sophisticated computer programs, which have had their validity checked against measured data. See Final Office Action, page 12.
>
> Mr. Wisniewski's guesswork even in declarative form is simply no substitute for real evidence. Neither he nor any other person on the planet is in a position to properly guess at the actual temperature distribution. See Final Office Action, page 14.

Accordingly, the Office admits that even those of ordinary skill in the art cannot look at and simply combine the cited references and arrive at the desired result disclosed in the Specification and recited in the claims of the present invention without experimentation or the aid of a computer.[5] In contrast, the explanations, schematics and temperature distributions provided by Mr. Wisniewski accompanying the First and

[5] However, the Examiner continues to ignore the disclosure in the Specification of the present invention which describes a simulation of the device conducted by Applicants (See Specification page 12) and that Applicants considered different gap sizes (See Specification page 6).

Second Wisniewski Declarations were supported by experimentation (e.g. see page 12 of the Specification) and knowledge of the devices, albeit limited memory of the device disclosed in the 1992 Wisniewski and Wu article. Therefore, the Office's combination of any of these references is improper based on its own admission and personal misunderstanding of this field of art.

1. Claims 88, 89, 96, 105, 108-110, 112-115, 118 and 119 Are Patentable Over the 1992 Wisniewski and Wu Article

Claims 88, 89, 96, 105, 108-110, 112-115, 118 and 119 stand rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over the 1992 Wisniewski and Wu article.

Each of the claims recite the formation of a "thermal bridge" such that "heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to "actively cooling" the interior wall. Admittedly, the Examiner states in the final Office Action "there is no explicit disclosure of any 'ice bridge' in the 1992 Wisniewski and Wu article."

The 1992 Wisniewski and Wu article discloses a device having an internal heat transfer coil pipe with fins welded to the external surface of the coil pipe. A copy of this device is reproduced, for convenience, below:

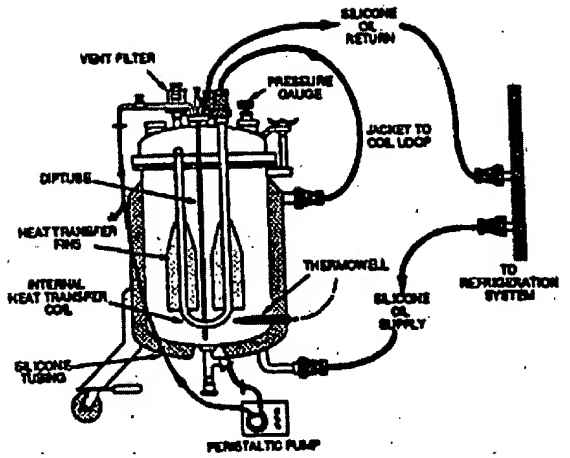

Figure 1. Freeze-thaw Vessel: Thawing Configuration

As shown, the fins attached to the pipe coil are very small and thin and were designed only to aid the freezing around the loop coil in order to increase the relatively small surface area of the loop pipe (e.g. adding more cold surface area). (Second Wisniewski Declaration, ¶8). The distance depicted in this drawing reasonably represented the relationship of the distance between the fins and the interior wall. Id. Mr. Wisniewski declared that this distance was greater than 4 inches. (Second Wisniewski Declaration, ¶8). The outside of this device is cooled.

The First Wisniewski Declaration, submitted during prosecution, provides schematic representations of the freezing which would have occurred in the device disclosed in the 1992 article at a period of time before the medium between the fin and the interior wall of the device is entirely frozen along with a graph showing the temperature distribution along the radius of the vessel. (See First Wisniewski Declaration, Exhibits B, C). As depicted in these schematic representations and graphs from the device disclosed in the 1992 article, the temperature in the gap between the fin and the interior wall increases and then decreases from the distal end of the fin to the interior wall. (First Wisniewski Declaration, ¶7). This temperature distribution occurs, in part, because the gap between the distal end of the fin and interior wall is too large. Id.

There is no discussion or suggestion in the 1992 Wisniewski and Wu article about the thermal bridges where heat is transferred from said heat transfer member through said thermal bridge to said interior wall as required by the claimed invention or the importance thereof in enhanced heat transport (See Specification at page 12, lines 9-16). In support of the rejection, the Examiner simply states, without any support thereof, that "[w]hile the 1992 article does not explicitly discuss a 'thermal bridge' there is nothing which suggests one did not form. The absence of any specific discussion is not necessarily evidence that the phenomena did not take place." (See final Office Action, page 9). However, the Examiner's mere speculation is insufficient to support this rejection, especially in view of the declarations and detail provided by the Appellant.

In the final Office Action, the Examiner states that a thermal "bridge of ice" will "inherently form" in the device disclosed in the 1992 Wisniewski and Wu article between the tip of the heat transfer member and the interior of the container because they are the closest points to one another and both are actively cooled by circulating cooled silicon oil and "closely spaced cooled surfaces are known by those of skill in the refrigeration art to form ice bridges when a liquid is being frozen into a solid. (page 11). In support of this statement, the Examiner points to the Voorhees, Burroughs and Finnegan patents. Appellant does not dispute that each of these references teach ice building up separately on different elements of the devices, e.g. fins and interior wall, and that this ice build-up meets in the space between the elements. Appellant understands that this is what the Examiner refers to as an "ice bridge." However, this freezing technique is not what is taught by the principles of the present invention and does not result in a downward temperature gradient from the fins to the interior wall as required by a thermal bridge where heat is transferred from said heat transfer member to the interior wall.

The Examiner's reliance on these references for an "ice bridge" demonstrates his failure to appreciate and/or understand the difference with what Appellant recite as a "thermal bridge" where heat is transferred from said heat transfer member to the interior wall. Appellant respectfully submits that the mere formation of ice about freezing

elements as, for example, disclosed in the Voorhees, Burroughs and Finnegan patents and the Examiner rendition of the device disclosed in the 1992 Wisniewski and Wu article on page 30 of the final Office Action, is not a "thermal bridge" in accordance with the principles of the present invention. In these examples, heat is not transferred from one freezing element through a thermal bridge to the other freezing element while the interior wall is actively cooled. Since there is ice build up on both the fin and the interior wall, then obviously the temperature at both of these locations is lower than the temperature at a located in between and there cannot be a downward temperature gradient where heat is transferred from the fin to the interior wall, as required by the formation of a thermal bridge. In contrast, with the Examiner's understanding of the formation of an "ice bridge", heat is transferred from a location in between the fin and interior wall and heat is transferred from this location to both the fin and the interior wall.

Burroughs, Finnegan and Voorhees fail to disclose or suggest the formation of a thermal bridge or motivate any modification of the device disclosed in the 1992 Wisniewski and Wu article so that a thermal bridge would form. In fact, each of these references teaches completely different methods of freezing products than the present invention and the 1992 Wisniewski and Wu article. For example, Burroughs is directed to freezing water in an ice trays that do not have an interior heat exchange structure, Finnegan is directed to a container for rapidly freezing comestibles to prevent fermentation, spoilage and concentration of sugar syrup, and Voorhees is directed to a device for freezing water having multiple cylindrical inserts and no external cooling jacket. Further, none of these references involve the processing of biopharmaceutical products and, therefore, fail to recognize the problems associated with processing such products. Therefore, there is no motivation in any of these references to combine with the 1992 Wisniewski and Wu article.

Even if the "same science" illustrated by Voorhees, Burroughs and Finnegan is applied to the system disclosed in the 1992 Wisniewski and Wu article to yield the results

illustrated on page 30[6] of the final Office Action as suggested by the Examiner, these results still do not result in the formation of a thermal bridge having a downward temperature gradient where heat is transferred through the medium from the fins to the interior wall of the device as required by the claims.

The Examiner also states that it would have been obvious to one of ordinary skill in the art to extend the fins in Figure 1 of the 1992 Wisniewski and Wu article to a point in close proximity to the interior surface of the container. See page 31 of Final Office Action. However, this article already teaches that the heat transfer fins "were configured to divide the tank volume into compartments to decrease freezing and thawing time and to reduce cryoconcentration effects." See pg. 136, col. 1. Thus, the 1992 Wisniewski and Wu article already teaches that the fins in the device aid in forming compartments and there is no motivation or suggestion in this article to further extend the fins further towards the walls.

For the above reasons, Appellant respectfully submits that the 1992 Wisniewski and Wu article fails to explicitly or inherently teach or suggest the claimed invention.

2. Claims 88, 89, 96, 105, 108-110, 112-115, 118 and 119 Are Patentable Over the 1992 Wisniewski and Wu Article in view of Euwema, Cothern, the 1986 Kalhori and Ramadhyani article, Morrison and Nakao

Claims 88, 89, 96, 105, 108-110, 112-115, 118 and 119 also stand rejected under 35 U.S.C. §103(a) as obvious over the 1992 Wisniewski and Wu article in view of Euwema, Cothern, the 1986 Kalhori and Ramadhyani article, Morrison and Nakao.

Section 103 of title 35 of the United States Code states:

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[6] The sketch illustrated on page 30 of the final Office Action shows ice build-up on both the fins and the interior wall of the device disclosed in the 1992 Wisniewski and Wu article.

> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertain.

In making the assessment of differences, section 103 specifically requires consideration of the claimed invention "as a whole". The "as a whole" instruction in title 35 prevents evaluation of the invention part by part.

The Federal Circuit provides assurance of an "as a whole" assessment of the invention under Section 103 by requiring a showing that an artisan of ordinary skill in the art at the time of invention, confronted by the same problems as the inventor and with no knowledge of the claimed invention, would select the various elements from the prior art and combine them in the claimed manner. *In re Rouffet*, 149 F.3d 1350, 1355-56, 47 U.S.P.Q.2d 1453 (Fed.Cir. 1998). In other words, the court must show some suggestion or motivation, before the invention itself, to make the new combination. Motivation to combine prior art references may be found in the nature of the problem to be solved.

None of these additional prior art references overcome the deficiencies of the 1992 Wisniewski and Wu article as applied against Appellant's claimed invention. Specifically, none of these additional prior art references disclose or suggest the formation of a "thermal bridge" such that "heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to "actively cooling" the interior wall, as required by the claims. Each of these references teach a completely different method of freezing products, using completely different principles that, especially in light of the Examiner's comments concerning the need for the assistance of computer assistance to determine temperature distribution, make combination of these references improper. Further none of these additional references are directed to the processing of biopharmaceutical products and, thus, fail to appreciate

the problems associated with processing these products and, thus, there is no motivation to combine.

a. Euwema

Euwema discloses a cooling tank having a central tank for cooling a quantity of carbonated liquid (not biopharmaceutical products), refrigeration chamber surrounding the central tank, and a precooling tank surrounding and connected to the refrigeration chamber. Abst. The carbonated liquid that is processed by Euwema is located within central tank 4. There are no heat transfer structures positioned within cooling tank 4. Therefore, no thermal bridge is formed by the carbonated liquid because there is no gap created between the interior wall of the central tank 4 and a heat transfer member since no heat transfer member exist within the tank 4. Moreover, since there are no structures in the cooling tank 4, a thermal transfer bridge does not form to conduct heat into or out of the liquid in the cooling tank 4. In the final Office Action, the Examiner relies on the freezing of a cooling fluid located in an outer pre-cooling tank 8. This precooling tank 8 has vanes 36 and 38 that are connected to the interior wall of a pre-cooling tank 8 and work to force the cooling fluid to be driven up and down as the fluid passes around the refrigeration chamber. The purpose of the fluid in the precooling tank is to provide relatively even cooling over the outer surface of the solidified precooling liquid. The cooling fluid in pre-cooling tank 8 and the refrigerant in refrigeration chamber 6 are not the desired product, i.e. carbonated liquid, to be cooled by the device disclosed in Euwema. Therefore, Euwema fails to cure the deficiencies of the 1992 Wisniewski and Wu article and, since they teach completely different methods using different principles, there is no motivation to combine these two references.

b. Cothern

Cothern is directed to a method and apparatus for freezing large blocks of a juice quickly (not biopharmaceutical product). Cothern discloses vessel 30 having freezing members 110 extending downwardly into the liquid within the vessel. Refrigerant flows through the freezing members 110 to provide a heat exchange mechanism for removing

heat from the liquid within the vessel. Since the freezing members have a lower temperature than the liquid within the vessel, e.g. between the tip of the freezing members and the interior wall, then the vessel disclosed in Cothern does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the vessel disclosed in Cothern has the reverse, i.e. an upward temperature gradient from the freezing members 110 to the interior wall of the vessel. Cothern fails to disclose or suggest the formation of a thermal transfer bridge that conducts heat into and out of the medium. Therefore, Cothern fails to cure the deficiencies of the 1992 Wisniewski and Wu article and, since they teach completely different methods using different principles, there is no motivation to combine these two references.

c. The 1986 Kalhori and Ramadyani Article

The 1986 Kalhori and Ramadyani article involves the investigation of the solidification of a paraffin[7] (not biopharmaceutical products) in a smooth, thin-walled metal cylindrical tank having an electrical strip heater wrapped around the upper part of the tank. The purpose of this investigation was to demonstrate that natural convection in the liquid phase plays a dominant role in melting and to a certain extent influences freezing. The investigation involves a comparison of the temperature distributions in the paraffin using a plain vertical cylinder in the tank and a vertical cylinder with fins, during cyclic melting and freezing. This cyclic cooling and heating generates convectional currents in the liquid phase of the medium. There is no disclosure or suggestion that the external tank walls are not actively cooled. In contrast, the vessel is wrapped with an electrical ban heater to warm the medium from the outside while the cylinder within is cooling it. Therefore, the temperature closer to the external wall from within the vessel increases, the temperature closer to the cylinder decreases, and heat transfer to the paraffin occurs from the cylinder.

[7] Paraffin is a white, waxy, odorless, tasteless solid substance consisting of a mixture of straight chais saturated hydrocarbon used to make, for example, candles, sealing preserving jars, waterproofing paper

The 1986 Kalhori and Ramadyani article simply concludes that the use of fins works better than no fins. However, this fact was already recognized in the 1992 Wisniewski and Wu article as shown by the disclosure of the coil pipe having fins attached thereto. Further, there is absolutely no disclosure or suggestion in the 1986 Kalhori and Ramadyani article of biopharmaceutical products or a discussion or recognition of the problems associated with processing biopharmaceutical product. Therefore, there is no motivation or suggestion to combine the 1986 Kalhori and Ramadyani article with the 1992 Wisniewski and Wu article because the 1986 Kalhori and Ramadyani article does not involve, or recognize the problems associate with processing, biopharmaceutical products.

There is also no motivation to combine the interior structure disclosed in the 1986 Kalhori and Ramadyani article with the container disclosed in the 1992 Wisniewski and Wu article because the devices disclosed in both articles involve different principles of freezing. Specifically, the device disclosed in the 1992 Wisniewski and Wu article cools the container from the outside and the inside and the 1986 Kalhori and Ramadyani article heats the container on the outside while cooling the container inside. Therefore, contrary to the Examiner's suggestion, it would not be obvious to simply put the finned cylinder disclosed in the 1986 Kalhori and Ramadyani article in the tank disclosed in the 1992 Wisniewski and Wu article because one of ordinary skill in the art would not be motivated to look towards the 1986 Kalhori and Ramadyani article to combine with the 1992 Wisniewski and Wu article due to problems associated with processing biopharmaceutical products and the fact that the device in the 1992 Wisniewski and Wu article already uses fins and cools the device from the inside using the coil pipe.

d. Morrison

Morrison is directed to a heat exchange device for use in heating or cooling liquids such as milk, or water or the like (not biopharmaceutical products). Similar to Cothern, the liquids are cooled in Morrison by a structure within the device. This structure includes hollow blades 7 that communications with a vertical chamber 6 so that

heat or cooling liquid circulates therethrough. There is no disclosure in Morrison that the walls of the container are "actively cooled." Since the hollow blades 7 and vertical chamber 6 have a lower temperature than the liquid within the Morrison device, e.g. between the tip of the freezing members and the interior wall, then the device disclosed in Morrison does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the Morrison device has the reverse, an upward temperature gradient from the freezing members 110 to the interior wall of the vessel. Morrison fails to disclose or suggest the formation of a thermal transfer bridge that conducts heat into and out of the medium. Therefore, Morrison fails to cure the deficiencies of the 1992 Wisniewski and Wu article and, since they teach completely different methods using different principles, there is no motivation to combine these two references.

e. Nakano

JP 57-58087 to Nakano is directed to a container for a heat-accumulating agent (not biopharmaceutical products). The Nakano container has metallic plates inserted within the container. The heat-accumulating agent 3 is fused due to heating, the heat of the fused part of the agent is transferred to the metallic plates 5 to heat the same. The arrows shown pointing to exterior surface of the container around its entire circumference appear to represent heat being applied to the exterior surface. With heat being applied to the outer surface of the container, there can be no downward temperature gradient from the tip of the metallic plates to the interior wall of the container because the temperature of the container wall is considerable higher than the tips of the metallic plates that transfers heat from the heat-accumulating agent 3. Nakano fails to disclose or suggest the formation of a heat transfer bridge as required by the claims of the present invention. Therefore, Nakao fails to cure the deficiencies of the 1992 Wisniewski and Wu article and, since they teach completely different methods using different principles, there is no motivation to combine these two references.

None of these references disclose or suggest the formation of a "thermal bridge." Moreover, since all of these devices teach different methods and principles of processing materials and do not deal with biopharmaceutical products or recognize the problems associated with processing the same, there is clearly no motivation or suggestion to combine any of these references with the 1992 Wisniewski and Wu article.

Accordingly, withdrawal of this ground of rejection and allowance of these claims are respectfully requested.

3. Claims 96, 105-110, 112-115, 118 and 119 Are Patentable Over The Combined Teachings Of The 1992 Wisniewski And Wu Article And The 1986 Kalhori And Ramadhyani Article

Claims 96, 105-110, 112-115, 118 and 119 also stand rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of the 1992 Wisniewski and Wu article and the 1986 Kalhori and Ramadhyani article

As discussed above, the 1986 Kalhori and Ramadyani article involves the investigation of the solidification of a paraffin[8] (not biopharmaceutical products) in a smooth, thin-walled metal cylindrical tank having an electrical strip heater wrapped around the upper part of the tank. The purpose of this investigation was to demonstrate that natural convection in the liquid phase plays a dominant role in melting and to a certain extent influences freezing. The investigation involves a comparison of the temperature distributions in the paraffin using a plain vertical cylinder in the tank and a vertical cylinder with fins, during cyclic melting and freezing. This cyclic cooling and heating generates convectional currents in the liquid phase of the medium. There is no disclosure or suggestion that the external tank walls are not actively cooled. In contrast, the vessel is wrapped with an electrical ban heater to warm the medium from the outside while the cylinder within is cooling it. Therefore, the temperature closer to the external

[8] Paraffin is a white, waxy, odorless, tasteless solid substance consisting of a mixture of straight chais saturated hydrocarbon used to make, for example, candles, sealing preserving jars, waterproofing paper

wall from within the vessel increases, the temperature closer to the cylinder decreases, and heat transfer to the paraffin occurs from the cylinder.

The 1986 Kalhori and Ramadyani article simply concludes that the use of fins works better than no fins. However, this fact was already recognized in the 1992 Wisniewski and Wu article as shown by the disclosure of the coil pipe having fins attached thereto. Further, there is absolutely no disclosure or suggestion in the 1986 Kalhori and Ramadyani article of biopharmaceutical products or a discussion or recognition of the problems associated with processing biopharmaceutical product. Therefore, there is no motivation or suggestion to combine the 1986 Kalhori and Ramadyani article with the 1992 Wisniewski and Wu article because the 1986 Kalhori and Ramadyani article does not involve, or recognize the problems associate with processing, biopharmaceutical products.

There is also no motivation to combine the interior structure disclosed in the 1986 Kalhori and Ramadyani article with the container disclosed in the 1992 Wisniewski and Wu article because the devices disclosed in both articles involve different principles of freezing. Specifically, the device disclosed in the 1992 Wisniewski and Wu article cools the container from the outside and the inside and the 1986 Kalhori and Ramadyani article heats the container on the outside while cooling the container inside. Therefore, contrary to the Examiner's suggestion, it would not be obvious to simply put the finned cylinder disclosed in the 1986 Kalhori and Ramadyani article in the tank disclosed in the 1992 Wisniewski and Wu article because one of ordinary skill in the art would not be motivated to look towards the 1986 Kalhori and Ramadyani article to combine with the 1992 Wisniewski and Wu article due to problems associated with processing biopharmaceutical products and the fact that the device in the 1992 Wisniewski and Wu article already uses fins and cools the device from the inside using the coil pipe.

Accordingly, withdrawal of this ground of rejection and allowance of these claims are respectfully requested.

4. Claims 96, 105-110, 112-115, 118 and 119 Are Patentable Over The Combined Teachings Of The 1992 Wisniewski And Wu Article And The 1986 Kalhori And Ramadhyani Article, Euwema, Cothern, West, Morrison and Nakao

Claims 96, 105-110, 112-115, 118 and 119 stand rejected under 35 U.S.C §103(a0 as being unpatentable over the combined teachings of the 1992 Wisniewski and Wu article, the 1986 Kalhori and Ramadhyani article, Euwema, Cothern, U.S. Patent No. 2,114,642 to West, Morrison and Nakao.

As discussed above, the 1986 Kalhori and Ramadhyani article, Euwema, Cothern, Morrison and Nakao references fail to overcome the deficiencies of the 1992 Wisniewski and Wu article as applied against Appellant's claimed invention. Specifically, none of these additional prior art references disclose or suggest the formation of a "thermal bridge" such that "heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to "actively cooling" the interior wall, as required by the claims. Each of these references teach a completely different method of freezing products, using completely different principles that, especially in light of the Examiner's comments concerning the need for the assistance of computer assistance to determine temperature distribution, make combination of these references improper. Further, none of these additional references are directed to the processing of biopharmaceutical products and, thus, fail to appreciate the problems associated with processing these products and, thus, there is no motivation to combine.

a. West

West also fails to overcome these deficiencies. West discloses an apparatus for accelerating the production of frozen articles, such as, milk, sherbets, ice creams, puddings and whipped cream (not biopharmaceutical products). Col. 4, lines 39-43. The West apparatus includes a cooling unit having an evaporator that provides a plurality of freezing units 4 adapted to receive and contain a refrigerant. The freezing units are

stationary and project down into the freezing chamber 5. The freezing chamber 5 is filled with a predetermined amount of liquid to be frozen. During freezing, the refrigerant will be condensed in a condenser 10 and accumulated in the receiver 11. The compressor 9 is started and evaporation of the refrigerant within the evaporator 3 causes rapid freezing of the contents of the containers because of the direct heat conductivity between the freezing members 4 and the substance to be frozen. Again, similar to Cothern and Morrison discussed above, the liquids are cooled in West by a structure within the device. Since the freezing member 4 has a lower temperature than the liquid within the West freezing container 8, e.g. between the tip of the freezing members and the interior wall, then the device disclosed in West does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the Morrison device has the reverse, an upward temperature gradient from the freezing member 4 to the interior wall of the container 8. Therefore, West fails to disclose or suggest the formation of a thermal transfer bridge that conducts heat into and out of the medium.

Accordingly, withdrawal of this ground of rejection and allowance of these claims are respectfully requested.

4. Claims 96, 105-110, 112-115, 118 And 119 Are Patentable Over Any Of The Prior Art As Applied Above For These Claims In View Of The Conceded Prior Art Discussed On Pages 1, Line 22 To Page 2, Line 17 Of The Specification

Claims 96, 105-110, 112-115, 118 And 119 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over any of the prior art as applied above for these claims in view of the conceded prior art discussed on pages 1, line 22 to page 2, line 17 of the specification.

During prosecution, Appellant submitted that the first two paragraphs in the Description of Prior Art section on page 2 of the specification refers to the device

disclosed in the 1992 Wisniewski and Wu article. (Second Wisniewski Declaration, ¶8). Therefore, as discussed above, this conceded prior art does not disclose or suggest the formation of a "thermal bridge" as required by the claims of the present invention.

The prior art described in the third paragraph of this section[9] refers to a device having ribs welded to both the core structure and the interior wall of the vessel. Such vessels can be used in storage devices for, e.g., paraffin. (Second Wisniewski Declaration, ¶9). During prosecution, Appellant directed the Examiner to two prior art patents, U.S. Patent Nos. 2,441,376 to Staining and 2,129,572 to Finnegan to show the type of devices mentioned in this part of the Specification. Since the ribs are connected to both the internal core and the interior wall of the vessel, no thermal bridge can be formed by the medium between a fin tip and the interior wall of the vessel (Second Wisniewski Declaration, ¶9). There is no gap between the ribs and the interior wall for a thermal bridge to form, as required by the claims of the present invention.

Accordingly, withdrawal of this ground of rejection and allowance of these claims are respectfully requested.

5. Claims 101, 111 and 116 Are Patentable Over Any Of The Prior Art As Applied Above To Claims 88, 110 and 115 Above, And Further In View Of Gross Or Brown

Claims 101, 111 and 116 stand rejected under 35 U.S.C. §103(a) as being unpatentable over any of the prior art applied to claims 88, 110 and 115 above, and further in view of Gross or Brown.

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[9] The statement by the Examiner in the final Office Action that Appellant "refused to provide a sketch" of this prior art device is without merit. Appellant directed the Examiner to a prior art references having similar features as discussed in this section. Clearly, it is not unduly burdensome to ask the Examiner to "imagine" the fins being secured to the interior wall of a device, which is completely irrelevant to the claims of the present invention because no "gap" for the formation of a "thermal bridge" can exist.

As discussed above, none of the prior art references cited by the Office disclose or suggest the formation of a "thermal bridge" such that "heat is transferred from said heat transfer member through said thermal bridge to said interior wall" in response to "actively cooling" the interior wall, as required by the claims. Each of these references teach a completely different method of freezing products, using completely different principles that, especially in light of the Examiner's comments concerning the need for the assistance of computer assistance to determine temperature distribution, make combination of these references improper. Further none of these additional references are directed to the processing of biopharmaceutical products and, thus, fail to appreciate the problems associated with processing these products and, thus, there is no motivation to combine. The Gross and/or Brown patents also fail to overcome these deficiencies.

a. Gross

Gross discloses a heat exchanger apparatus for facilitating the transfer of heat through heat-conducting walls of the apparatus by the circulation of fluid heat-transfer medium in contact with the heat-conducting walls. Abst. The heat exchanger apparatus has a cavity defining heat-conducting wall 1 that houses a casing 10 formed of a flexible material with partitions 15 which are integral with the casing 10. Casing 10 is inserted into the cavity within the heat-conducting wall 1. Edges 16 of partitions 15 are resiliently pressed against the inner surface 2 of wall 1. Col. 4, lines 5-16. The "means forming spiral paths on the outside of a tank" referred to by the Examiner in the Final Office Action (page 48) in Gross are brackets 216 or spacers 215 that assist in supporting the kettle, not baffles within the fluid flow path between a jacket and the exterior wall of the apparatus to define a spiraling path for fluid, as required by the claims.

b. Brown

Brown discloses a material-treating tank to heat or cool plastic mixtures or fluid, for instance, in dairy processing and chemical plants. Col. 1, lines 10-13. The tank disclosed in Brown has a jacket surrounding the tank, which facilitates the circulation of fluid heat exchange medium. There are no internal heat transfer structures contained

within the tank. Therefore, a "thermal bridge" does not form between a heat exchange structure and the interior wall of the tank, as required by the claims of the present invention. Brown teaches a completely different method of freezing products, using completely different principles that, especially in light of the Examiner's comments concerning the need for the assistance of computer assistance to determine temperature distribution, make combination of this reference improper. Further Brown is not directed to the processing of biopharmaceutical products and, thus, fails to appreciate the problems associated with processing these products and, thus, there is no motivation to combine.

Accordingly, withdrawal of this ground of rejection and allowance of these claims are respectfully requested.

C. Appellant Satisfied Its Duty Under Rule 56

Throughout the prosecution of this application, the Examiner requested additional information concerning the prior art devices disclosed in the specification and the Genentech device disclosed in the 1992 disclosure of Wisniewski and Wu. The Examiner also suggested that the inventors contact Genentech to obtain the dimensions of the prior art Genentech device. However, the Examiner assumed that the Appellant was in possession of this information because they worked on the Genentech device more than a decade ago. Moreover, the Examiner has made this request even when the 1992 Wisniewski and Wu article depicts the known prior art.

In Appellant's response dated October 7, 2002, appellant made clear to the Examiner that the applicants do not work for Genentech and are not in possession of the 1992 Genentech device. In an effort to further assist the Office, one of the inventors, Mr. Wisniewski, submitted a Second Declaration that provided as much information that he could remember concerning the Genentech device. Appellant makes no admission that any device made by Genentech constitutes prior art within the meaning of 35 U.S.C. §102. Appellant recognizes, however, that the 1992 Wisniewski and Wu article, which depicts a device made by Genentech, does qualify as prior art under 35 U.S.C. §102(b).

Therefore, the Examiner merely speculates that Mr. Wisniewski has a "close connection to Genentech."

Appellant promptly responded to any request from the Examiner and explained numerous times that it has disclosed as much information as it can remember concerning the Genentech device. Moreover, the device is depicted in the 1992 Wisniewski and Wu article cited to by the Examiner. Therefore, Appellant has satisfied their duty under Rule 56 and the Office should have considered Appellant's response to the third Office Action as a complete reply under 37 C.F.R. §1.105(a)(3).

Appellant provided the Office with as much information concerning the prior art that is presently know or readily available. Mr. Wisniewski, co-author of the 1992 article has unequivocally stated that a thermal bridge where heat is transferred from the heat transfer member to the interior wall of the vessel was not disclosed in the 1992 article and did not occur in the Genentech device. Whether or not Genentech is a competitor or customer (both are actually true), Rule 56 does not require an applicant to contact another company for a competitive device in order to conduct experiments using its own equipment to perform testing to support the Examiner's unsupported beliefs and speculation, which have no bearing upon the claims. Clearly, this request exceeds the requirement under Rule 56.

Therefore, Appellant respectfully submits that all information that is known and readily available has been disclosed.

Conclusion

For the reasons set forth above, reversal of the rejections and allowance of this application are respectfully requested.

Dated: June 10, 2004

Respectfully submitted,

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APPENDIX

CLAIMS FOR APPLICATION SERIAL NUMBER 08/895,936

88. A method of processing a biopharmaceutical product comprising:

providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, said vessel having an interior cavity defined by an interior wall of said vessel and a heat exchange structure within said cavity, said heat exchange structure having one or more heat transfer members;

placing a medium comprising a biopharmaceutical product within said vessel;

actively cooling said interior wall using a cooling fluid; and

forming a thermal bridge within a gap between said heat transfer members and said interior wall by said medium wherein heat is transferred from said heat transfer member through said thermal bridge to said interior wall.

89. The method of claim 88, further comprising:

actively cooling said heat exchange structure using a cooling fluid.

96. The method of claim 88, wherein said heat transfer members are fins.

101. The method of claim 88, further comprising:

positioning baffles within the fluid flow path between the jacket and the exterior wall of said vessel to define a spiraling path for fluid.

105. The method of claim 88, wherein the heat exchange structure comprises a plurality of heat transfer members, said plurality of heat transfer members being configured within said interior cavity to form freezing compartments.

106. The method of claim 105, wherein said freezing compartments are formed between adjacent heat transfer members and said interior wall.

107. The method of claim 88, wherein said heat exchange structure comprises a pipe being positioned in the center of said interior cavity, said heat transfer members extend radially from said pipe.

108. A method of processing a biopharmaceutical product comprising:

placing a medium comprising a biopharmaceutical product within a vessel having an interior cavity defined by an interior wall of said vessel and a heat exchange structure within said cavity, said heat exchange structure having one or more heat transfer members;

actively cooling said interior wall using a cooling fluid; and

forming a thermal bridge within a gap between said heat transfer members and said interior wall by said medium wherein heat is transferred from said heat transfer member through said thermal bridge to said interior wall.

109. The method of claim 108 further comprising storing the medium in the vessel after being actively cooled.

110. The method of claim 108, wherein said vessel comprises a jacket spaced from an exterior wall of said vessel to define a fluid flow path adapted to receive fluid to actively cool said interior wall.

111. The method of claim 110 further comprising placing baffles within the fluid flow patch between the jacket and the exterior wall of said vessel to define a spiraling path for fluid.

112. The method of claim 108, wherein said heat exchange structure is removable from said vessel.

113. The method of claim 108, wherein the heat exchange structure comprises a plurality of heat transfer members, said plurality of heat transfer members being configured within said interior cavity to form freezing compartments.

114. A method of facilitating the processing of a biopharmaceutical product comprising:

providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, said vessel having an interior cavity defined by an interior wall of said vessel and a heat exchange structure within said cavity, said heat exchange structure having one or more heat transfer members; and

providing a passage for actively cooling said interior wall using a cooling fluid to form a thermal bridge within a gap between said heat transfer members and said interior wall by said medium wherein heat is transferred from said heat transfer member through said thermal bridge to said interior wall.

115. The method of claim 114, wherein said vessel comprises a jacket spaced from an exterior wall of said vessel to define a fluid flow path adapted to receive fluid to actively cool said interior wall.

116. The method of claim 115 further comprising providing baffles within the fluid flow path between the jacket and the exterior wall of said vessel to define a spiraling path for fluid.

118. The method of claim 114, wherein said heat exchange structure comprises a plurality of heat transfer members.

119. The method of claim 118, wherein said plurality of heat transfer members being configured within said interior cavity to form freezing compartments.